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What is claimed is:

1. A compound of a formula I:

wherein Z is

H; A"; B"; or

n, m, q and r are independently integers from zero to 4 provided that  $n + m \le 4$  and  $q + r \le 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \le 5$ ; a, b and c are double bonds which may be present or absent;

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when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

- R, R' and R" are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', wherein Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R", -NH<sub>2</sub>, -NHR", -NR<sub>2</sub>", -OH, -OR", halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R" is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl.
  - A, A' and A" are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C₁-C₂₀ acyloxy; C\-C₂₀ alkanoyl;

 $C_1$ - $C_{20}$  alkoxycarbonyl;  $C_1$ - $C_{20}$  alkoxy;

 $C_1$ - $C_{20}$  alkylamino;  $C_1$ - $C_{20}$  alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

B, B' and B" are independently H;

 $C_1$ - $C_{20}$  acylamino;  $C_1$ - $C_{20}$  acyloxy;  $C_1$ - $C_{20}$  alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

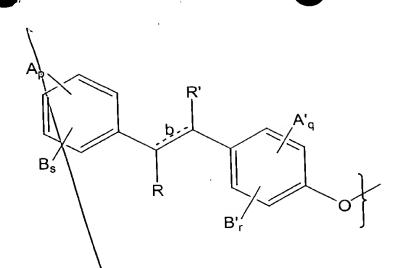
 $C_1$ - $C_{20}$  alkoxy;  $C_1$ - $C_{20}$  alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamind; aroyl, aralkanoyl; carboxyl; cyano; halo; hydroxy;

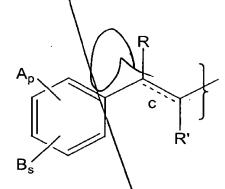
or A and B together, or A' and B' together, or A" and B" together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR", O of S.

2. A compound according to claim \( \), wherein Z is

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- 3. A compound according to claim 1, wherein Z is hydrogen.
- 4. A compound according to claim 1, wherein Z is A".
- 5. A compound according to claim 1, wherein Z is B".
- 6. A compound according to claim 1, wherein Z is



- 7. A compound according to claim 2; wherein X is sulfur, X' is -NH; A"n, B", B', Ap, A'q, R and R" are all hydrogen.
- 8. A compound according to claim 3, wherein B is methoxy, s is 2 and R' is carbomethoxy.

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- 9. A compound according to claim 8, which is 5-(4-(4-(1-carbomethoxy-2-(3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.
- 10. A pharmaceutical composition comprising a therapeutically effective amount of a compound of the formula I:

wherein Z is

H; A"; B"; or

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n, m, q and r are independently integers from zero to 4 provided that  $n + m \le 4$  and  $q + r \le 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \le 5$ ; a, b and c are double bonds which may be present or absent; when present the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;

Inear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>''', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl,

15 A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

 $C_1$ - $C_{20}$  acyloxy;  $C_1$ - $C_{20}$  alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano;

halo; hydroxy;

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B, B' and B" are independently H;

C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

25 C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

hydroxy;

or A and B together, or A' and B' together, or A" and B" together, may be joined to form a methylenedioxy or ethylenedioxy group; and

X, X' are independently -NH, -NR", O or S.

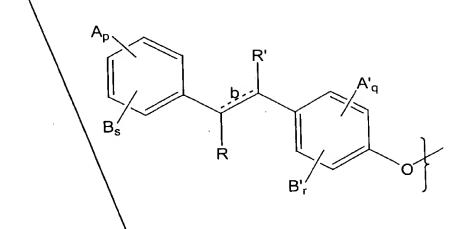
30 in a physiologically acceptable carrier.

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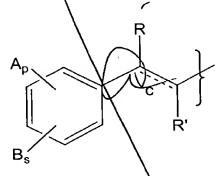
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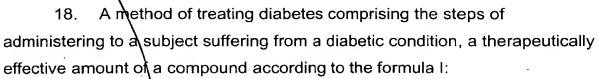
11. A composition according to claim 10, wherein Z is

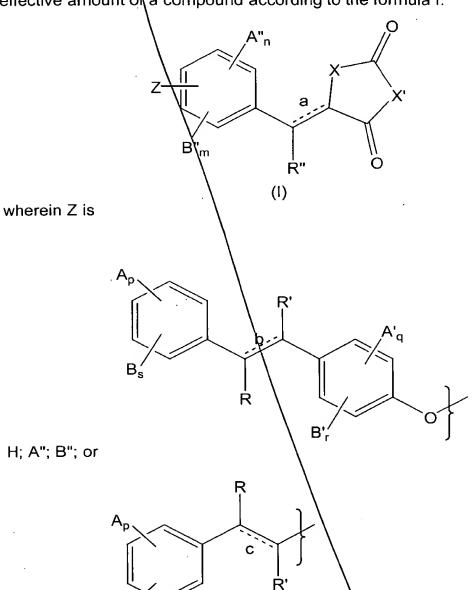


- 12. A composition according to claim 10, wherein Z is A".
- 13. A composition according to claim 10, wherein Z is B".
- 14. A composition according to claim 10, wherein Z is



- 15. A composition according to claim 10, wherein X is sulfur, X' is -NH and A", B", A'<sub>q</sub>, B', A<sub>p</sub>, R and R" are all hydrogen.
- 16. A composition according to claim 15, wherein R' is carbomethoxy; B is methoxy and s is 2.

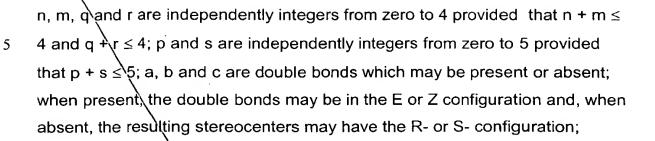




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- 10 R, R' and R" are independently H, C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl, C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, -CO<sub>2</sub>Z', where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; -CO<sub>2</sub>R''', -NH<sub>2</sub>, -NHR''', -NR<sub>2</sub>''', -OH, -OR''', halo, substituted C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or substituted C<sub>2</sub>-C<sub>20</sub> linear or branched alkenyl, wherein R''' is C<sub>1</sub>-C<sub>20</sub> linear or branched alkyl or linear or branched alkenyl;
  - A, A' and A' are independently H,  $C_1$ - $C_{20}$  acylamino;

 $C_1$ - $C_{20}$  acyloxy;  $C_1$ - $C_{20}$  alkanovl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

B, B' and B" are independently H;

C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

 $C_1\text{-}C_{20}$  alkenoyl;  $C_1\text{-}C_{20}$  alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo; hydroxy;

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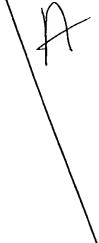
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or A and B together, or A' and B' together, or A" and B" together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR", O or S, in a physiologically acceptable carrier.

19. A method according to claim 18, wherein Z is

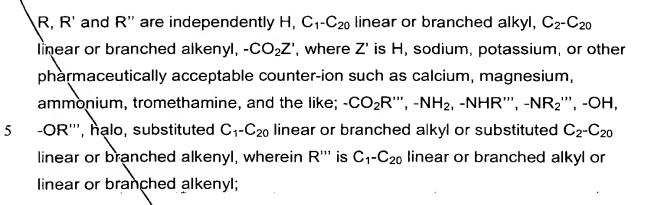
- 20. A method according to claim 19, wherein Z is H.
- 21. A method according to claim 18, wherein Z is A".
- 22. A method according to alaim 1,8, wherein Z is B".
- 23. A method according to claim 18, wherein Z is

- 24. A method according to claim 18, wherein R", A", B", A'<sub>q</sub>, B', A<sub>p</sub> and R are all hydrogen, X is sulfur and X' is NH.
- 25. A method according to claim 18, wherein R" is carbomethoxy and B is methoxy and s is 2.
  - 26. A method according to claim 18, wherein said compound is 5-(4-(4-(1-carbomethoxy-2-)3,5-dimethoxy phenyl) ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.
  - 27. A method of treating inflammation comprising the steps of administering to a subject suffering from an inflammatory condition, a therapeutically effective amount of a compound according to the formula I:



(1) wherein Z is R В H; A"; B"; or

n, m, q and r are independently integers from zero to 4 provided that n + m  $\leq$  4 and q + r  $\leq$  4; p and s are independently integers from zero to 5 provided that p + s  $\leq$  5; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration;



A, A' and A" are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

 $C_1$ - $C_{20}$  alkylamino;  $C_1$ - $C_{20}$  alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

15 B, B' and B" are independently H;

 $C_1$ - $C_{20}$  acylamino;  $C_1$ - $C_{20}$  acyloxy;  $C_1$ - $C_{20}$  alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

 $C_1$ - $C_{20}$  alkoxy;  $C_1$ - $C_{20}$  alkylamino)

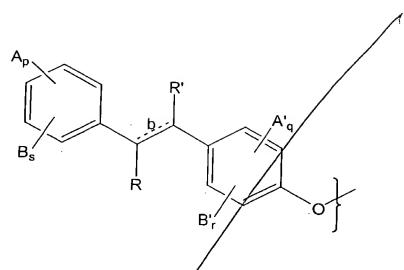
C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; atoxil, aralkanoyl; carboxyl; cyano; halo;

20 hydroxy;

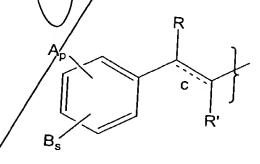
or A and B together, or A' and B' together, or A' and B' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR", O or S, in a physiologically acceptable carrier.

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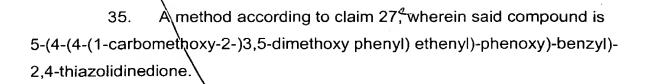
28. A method according to claim 27, wherein \( \begin{align\*} \pi \) is



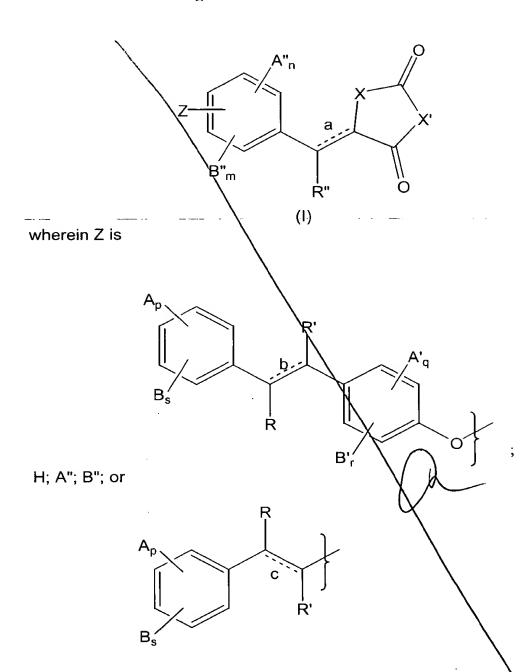
- A method according to claim 27 wherein Z is H. 29.
- A method according to claim 27, wherein Z is A". 30.
- A method according to claim 27, wherein Z is B". 31.
- A method according to claim 27, wherein Z is 32.



- method according to claim 27, wherein R", A", B", A'<sub>q</sub> B', 33. Ap and R are all hydrogen, X is sulfur and X' is NH.
- A method according to claim 33, wherein R' is carbomethoxy 15 and B is methoxy and s is 2.



36. A method of treating immunological disease comprising the steps of administering to a subject suffering from an immunological disease, a therapeutically effective amount of a compound according to the formula I:



n, m, q and r are independently integers from zero to 4 provided that  $n + m \le 4$  and  $q + r \le 4$ ; p and s are independently integers from zero to 5 provided that  $p + s \le 5$ ; a, b and c are double bonds which may be present or absent; when present, the double bonds may be in the E or Z configuration and when absent, the resulting stereocenters may have the R- or S- configuration;

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R, R' and R" are independently H,  $C_1$ - $C_{20}$  linear or branched alkyl,  $C_2$ - $C_{20}$  linear or branched alkenyl, - $CO_2Z'$ , where Z' is H, sodium, potassium, or other pharmaceutically acceptable counter-ion such as calcium, magnesium, ammonium, tromethamine, and the like; - $CO_2R'''$ , - $NH_2$ , -NHR''', - $NR_2'''$ , -OH, -OR''', halo, substituted  $C_1$ - $C_{20}$  linear or branched alkyl or substituted  $C_2$ - $C_{20}$  linear or branched alkenyl, wherein R''' is  $C_1$ - $C_{20}$  linear or branched alkenyl;

A, A' and A'' are independently H, C<sub>1</sub>-C<sub>20</sub> acylamino;

 $C_1$ - $C_{20}$  acyloxy;  $C_1$ - $C_{20}$  alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl; C<sub>1</sub>-C<sub>20</sub> alkoxy;

C<sub>1</sub>-C<sub>20</sub> alkylamino; C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; carboxyl; cyano; halo; hydroxy;

15 B, B' and B" are independently H,

C<sub>1</sub>-C<sub>20</sub> acylamino; C<sub>1</sub>-C<sub>20</sub> acyloxy; C<sub>1</sub>-C<sub>20</sub> alkanoyl;

C<sub>1</sub>-C<sub>20</sub> alkenoyl; C<sub>1</sub>-C<sub>20</sub> alkoxycarbonyl;

C<sub>1</sub>-C<sub>20</sub> alkoxy; C<sub>1</sub>-C<sub>20</sub> alkylamino;

C<sub>1</sub>-C<sub>20</sub> alkylcarboxylamino; aroyl, aralkanoyl; carboxyl; cyano; halo;

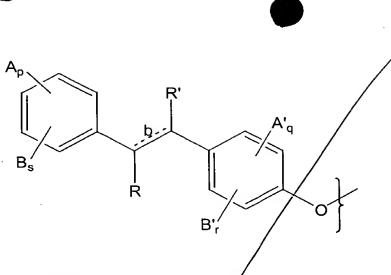
20 hydroxy;

or A and B together, or A' and B' together, or A" and B" together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR", O or S, in a physiologically acceptable carrier.

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37. A method according to claim 36, wherein Z is

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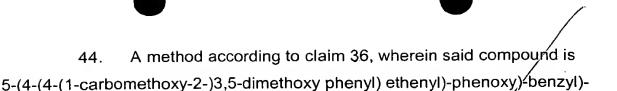
- 38. A method according to claim 36, wherein Z is H.
- 39. A method according to claim 36, wherein Z is A".
- 40. A method according to claim, 36; wherein Z is B".
- 41. A method according to claim 36, wherein Z is

- 42. A method according to claim 36, wherein R", A", B", A'<sub>q</sub>, B', A<sub>p</sub> and R are all hydrogen, X is sulfur and X' is NH.
- 43. A method according to claim 42, wherein R' is carbomethoxy and B is methoxy and s is 2.

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5 45. A method of inhibiting the activity of TNF-alpha, IL-1, IL-6 or COX-2 which comprises administering to a host in need of such inhibition an

effective amount of a compound according to claim 1.

2.4-thiazolidinedione.

- 46. The method of treating inflammation, inflammatory or immunological disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.
  - 47. The method of inhibiting the undesired action of cytokine or cyclooxygenase which comprises administering to a host in need of such inhibition an effective amount of a compound according to claim 1.
  - 48. The method of freating an inflammatory disease mediated by cytokines or cyclooxygenase which comprises administering to a host in need of such treatment a compound according to claim 1.
  - 49. The method of treating insulin resistance which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.
- 25 50. The method of treating hyperlipidemia which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.
  - 51. The method of treating coronary heart disease which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.



52. The method of treating multiple sclerosis which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

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53. The method of treating cancer which comprises administering to a host in need of such treatment an effective amount of a compound according to claim 1.

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54. The method of claim 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein the compound is 5-(4-(4-(1-carbomethoxy)-2-(3,5-dimethoxyphenyl)-ethenyl)-phenoxy)-benzyl)-2,4-thiazolidinedione.

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55. A compound according to claim 1 selected from the group consisting of:

3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propjonic acid,

30 3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)--phenoxy]<sub>7</sub>phenyl}-propionic acid,

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3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid, and 3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid methyl ester.

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56. A compound according to claim 1 which is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.

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57. A pharmaceutical composition comprising a therapeutically effective amount of a compound selected from the group consisting of 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-{4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{\dagger}-[4/(2/,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)—phenoxy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid methyl ester,

3-(3,5-dimethoxy-phényl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic/acid,

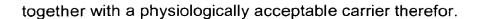
3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid, and

30 3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid methyl ester,

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- 58. The pharmaceutical composition of claim 57 wherein/said compound is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.
- 59. The method of claim 18, 45, 46, 47, 48, 49, 50, 51, 52 or 53 wherein said compound is selected from the group consisting of 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N,N-dimethyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-N-methoxy,-N-methyl-acrylamide,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenyy]-phenyl}-propionic acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic/acid methyl ester,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic agid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-propionic acid,

3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylidenemethyl)-phenoxy]-phenyl}-acrylic acid, and 3-(3,5-dimethoxy-phenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-propionic acid methyl ester.



as compound is 3 (3.5

60. The method of claim 59 wherein the compound is 3-(3,5-dimethoxyphenyl)-2-{4-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-phenyl}-acrylic acid.

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